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Genetic Alterations in Psoriasis

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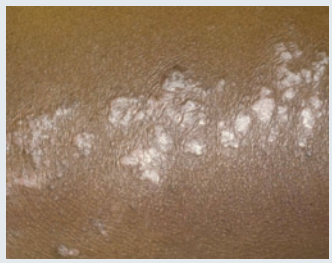

The genetic basis of psoriasis has long been recognized, including the knowledge that family members of patients with psoriasis are at greater risk of developing the disease (Henselers and Christophers, 1995). Several lines of evidence suggest that genes regulating IL-12 and IL-23 may be important in its pathogenesis. Part of the rationale stems from observations indicating that patients with psoriasis and those with Crohn's disease share common features: patients with Crohn's disease are five times more likely than the general population to have psoriasis, and both diseases respond to anti–tumor necrosis factor-α therapy (Lee *et al*., 1990). A recent genome-wide association scan identified a highly significant association between Crohn's disease and a single-nucleotide polymorphism (SNP) in the coding region of the *IL23R* gene (Duerr *et al*., 2006), suggesting that this polymorphism might be present in patients with psoriasis. Additional studies from several diverse ethnic populations throughout the world have determined that psoriasis is associated with SNPs in IL-12 and IL-23 or their receptors (Capon *et al*., 2007; Cargill *et al*., 2007; Chang *et al*., 2007; Tsunemi *et al*., 2002).

On the basis of the above information, Nair *et al*. (2008) studied four candidate SNPs in a large (more than 4,000 persons) cohort of white North American and German subjects with psoriasis and in controls. Two of the SNPs were the *IL12B* haplotype rs3212227 and rs6887695; the other two were *IL23R* haplotype rs7530511 and rs11209026. Nair *et al*. found that both *IL12B* markers had a highly significant association with psoriasis (odds ratio (OR) 1.62 and 1.49 for rs3212227 and rs6887695, respectively). The *IL23R* SNPs also demonstrated significant associations in the cases and controls (OR 1.22 and 1.40 for rs7530511 and rs11209026, respectively). These SNPs were not found to have interactions with a known genetic risk factor, *HLA-Cw6*.

Through the following questions, we examine this paper in greater detail. For brief answers, please refer to http://network.nature.com/group/jidclub.

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QUESTIONS

1. What is a single-nucleotide polymorphism (SNP)?
2. What data support an association between Crohn's disease and psoriasis?
3. Why are *IL12B* and *IL23R* candidates for study?
4. How was the study performed?
5. What were the major findings of this study?
6. What may be the clinical implications of this study, and how may they change the way we think about the genetics of psoriasis?
7. What future studies might extend these findings?

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